Lorcaserin did not Increase the Rate of Neoplasia Adverse Events in Pooled Phase 3 Studies, Year 1

n(%) of patients	Placebo N=3185		Lorcaserin N=3195	
	n	%	n	%
Total Number of Events	**30**	**0.9%**	**28**	**0.9%**
Basal cell carcinoma	12	0.4	4	0.1
Breast cancer	4	0.1	4	0.1
Thyroid neoplasm	6	0.2	3	0.1
Lung adenocarcinoma	0	-	2	0.1
Multiple myeloma	0	-	2	0.1
Prostate cancer	3	0.1	2	0.1
Breast cancer in situ	0	-	1	<0.1
Carcinoid tumor (of appendix)	0	-	1	<0.1
Lung neoplasm	1	<0.1	1	<0.1
Malignant melanoma	2	0.1	1	<0.1
Nasopharyngeal cancer	0	-	1	<0.1
Rectal neoplasm	0	-	1	<0.1

Lorcaserin Did Not Increase Neoplasia Adverse Events – Years 1 and 2, Both Studies

Terms Reported by >1 Patient in Any Group

	Placebo N=3185		Lorcaserin BID* N=3195	
Preferred Term	**n**	**%**	**n**	**%**
Total Patients, ALL neoplasm terms	**73**	**2.3**	**79**	**2.5**
Uterine leiomyoma	11	0.3	18	0.6
Basal cell carcinoma	12	0.4	9	0.3
Breast cancer	4	0.1	5	0.2
Thyroid neoplasm (nodules)	6	0.2	5	0.2
Prostate cancer	3	0.1	3	0.1
Lung adenocarcinoma	0	0	2	0.1
Multiple myeloma	0	0	2	0.1
Neuroma	1	<0.1	2	0.1
Skin cancer	0	0	2	0.1
Malignant melanoma	2	0.1	1	<0.1
Squamous cell carcinoma	2	0.1	1	<0.1
Bladder cancer	3	0.1	0	0

*Year 2 events in lorcaserin/placebo group counted as lorcaserin. Excludes wart, naevus, lipoma, hemangioma.

Independently Adjudicated Ischemic Cardiovascular Events in Phase 3 Studies

Adjudicated Term n(%)	APD356-009 PBO N=1584	APD356-009 LOR BID N=1593	APD356-011 PBO N=1601	APD356-011 LOR BID N=1602	Pooled Phase 3 PBO N=3185	Pooled Phase 3 LOR BID N=3195
TOTAL CARDIOVASCULAR	3	1	3	4	6	5
Total Cardiac	2	1	1	4	3	5
Total Cerebrovascular	1	-	2	-	3	-
MI, spontaneous	-	-	-	4	-	4
MI, silent	1	-	-	-	1	-
Unstable angina, hospitalization*	1	1	1	-	2	1
Cardiac deaths	-	-	-	-	-	-
Stroke, ischemic	-	-	1	-	1	-
TIA	1	-	1	-	2	-
Stroke deaths	-	-	-	-	-	-

*1 additional patient assigned to lorcaserin/placebo had unstable angina during Year 2 (Day 643) while taking placebo

Piecewise Exponential Model: Parameterization

- Study = 1 if 009; 0, otherwise
- Year = 1 if Year 2 009; 0 if Year 1 for 009, 011
- Q2 = 1 if Week 24 to 52 of Year 1; 0, otherwise
- Q4 = 1 if Week 24 to 52 of Year 2; 0, otherwise
- T1 = 1 if Lorcaserin in Year 1 of 009 or 011;
  0, otherwise
- T2 = 1 if Lorcaserin in Year 2 of 009, 0, otherwise
- P2 = 1 if Placebo in Year 2 AND Pbo/Pbo group
  0, otherwise
- TS = 1 if Lorcaserin Year 1 of 011; 0, otherwise.

Piecewise Exponential Model: Simplification

- Test for Treatment by Study
  - Model: Study Year Q2 Q4 T1 T2 P2 TS
  - TS term is not significant (p = 0.935)
- Test for Ho: T1 = T2
  - Model: Study Year Q2 Q4 T1 T2 P2
  - Contrast: T1 vs T2 is not significant (p=0.704)
- Test for Ho:P2=0
  - Model: Study Year Q2 Q4 T P2
  - P2 term is not significant (p=0.505)

Piecewise Exponential Model: Simplification

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  - Model: Study Year Q2 Q4 T1 T2 P2 TS
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  - Model: Study Year Q2 Q4 T1 T2 P2
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- Test for Ho:P2=0
  - Model: Study Year Q2 Q4 T P2
  - P2 term is not significant (p=0.505)

Models Considered: Goodness of Fit

Model	df	Pearson Chi-square	P-value
Study+Year+Q2+Q4+T+P2	7	2.74	0.908
Study+Year+Q2+Q4+T	8	3.17	0.923
T	12	14.80	0.253

Simplified Model: T
FDA-defined valvulopathy Rate per Year

Treatment	FDA-defined valvulopathy Rate per Year	95% CI	Rate Ratio (95% CI)
Lorcaserin	0.035	(0.028, 0.041)	1.05 (0.79, 1.40)
Placebo	0.033	(0.026, 0.039)	

GEE Method for Simplified Model: T FDA-defined Valvulopathy Rate

Treatment	FDA-defined valvulopathy Rate	95% CI	Rate Ratio (95% CI)
Lorcaserin	0.0234	(0.019, 0.029)	1.02 (0.76, 1.38)
Placebo	0.0229	(0.018, 0.028)	

Simplified Model: T
Probability of an Event by 1 Year

Treatment	Probability of an Event by 1Year	95% CI	Risk Ratio (95% CI)
Lorcaserin	0.034	(0.028,0.041)	1.05 (0.79, 1.39)
Placebo	0.032	(0.026, 0.039)	

Changes in Apolipoprotein APD356-011

	Placebo n=520	10 mg QD n=267	10 mg BID n=580
Apo A1			
Mean (SD) Baseline (mg/dL)	147.3 (23.4)	149.2 (24.2)	147.3 (24.7)
Mean (SEM) % Change	-0.4 (0.5)	-0.7 (0.7)	-0.2 (0.5)
P-value		0.1798	0.7604
Apo B			
Mean (SD) Baseline (mg/dL)	90.6 (20.2)	91.3 (19.7)	91.2 (22.4)
Mean (SEM) % Change	1.4 (0.7)	-0.5 (0.7)	-2.9 (0.7)
P-value		0.1227	<0.0001

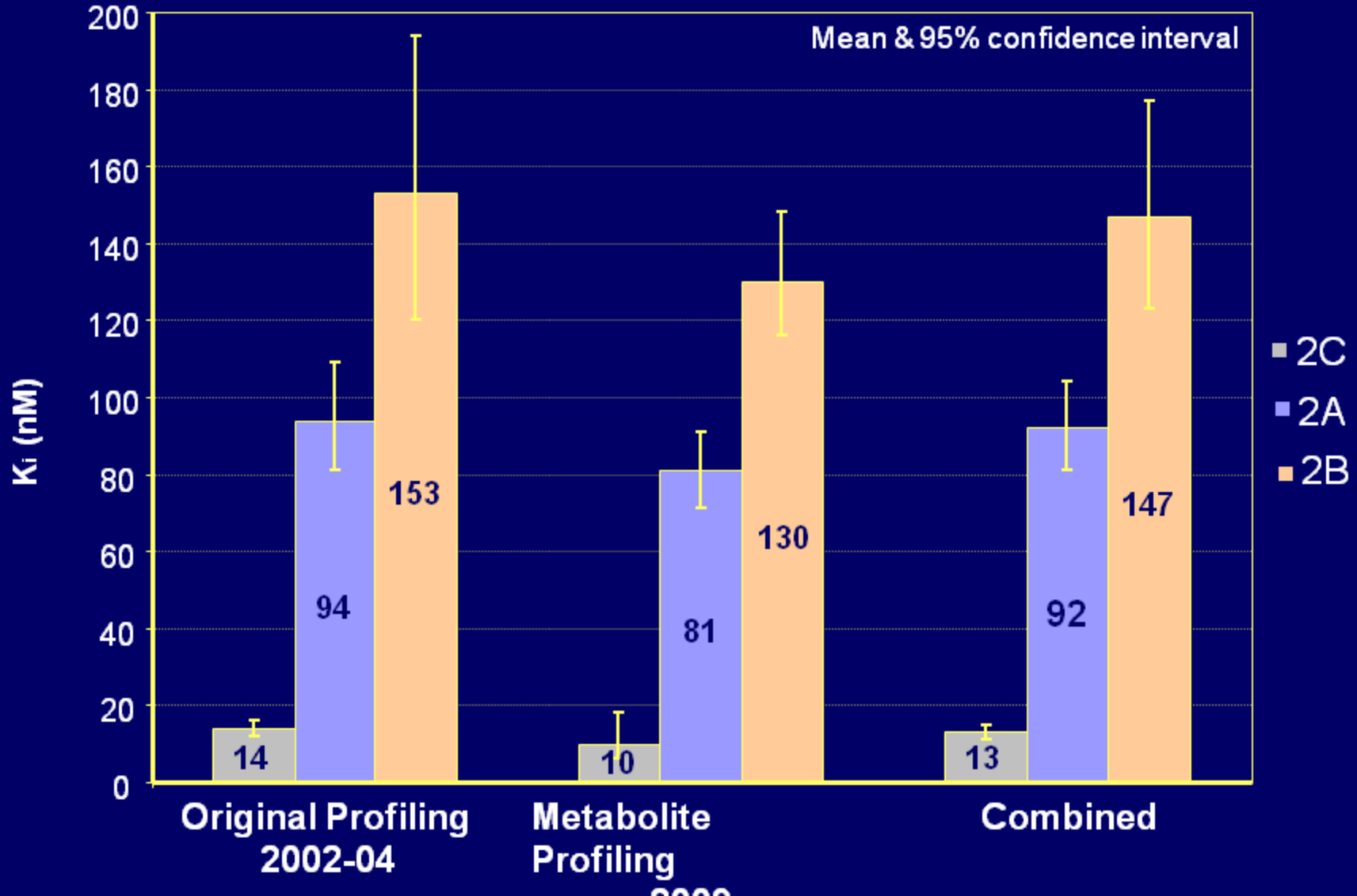
Changes in Concomitant Medications for Hypertension or Dyslipidemia in Pooled Phase 3 Studies

n(%) of patients	Pooled	
	Placebo (N=3185)	Lorcaserin 10 mg BID (N=3195)
Anti-hypertensive medications		
Decrease	54 (1.7)	70 (2.2)
No change	595 (18.7)	594 (18.6)
Increase	95 (3.0)	70 (2.2)
New initiation	44 (1.4)	35 (1.1)
Anti-dyslipidemia medications		
Decrease	23 (0.7)	43 (1.3)
No change	474 (14.9)	484 (15.1)
Increase	109 (3.4)	83 (2.6)
New initiation	80 (2.5)	62 (1.9)

Reproductive Toxicology Summary of Results

Dose (mg/kg/day)	Results	
Segment I/ Fertility and Early Embryonic Development		
0, 5, 15, 50	Males:	100% fertile, 100% mated
	Females:	No effect on estrus cycle length Pregnancy: 20/20 (5 mg/kg); 19/20 (15 and 50 mg/kg) No lorcaserin effect on resorptions, live conceptuses, or post-implantation losses No effect on litter size, live fetuses, resorptions, fetal weight, sex ratios, of gross anatomy
Segment II/ Embryo-Fetal Development		
30, 100, 300	Dams:	Decreased food intake (300 mg/kg/day); decreased body weight (100 and 300 mg/kg) No effect on implantations
	Litters:	No effect on litter size, resorptions, number of dead fetuses, sex ratios
Segment III/ Pre- and Post-Natal Development		
0, 5, 15, 50	F0:	Clinical findings at 15 and 50 mg/kg; decreased food consumption at all doses
	F1:	No effect on litter size, number of liveborn pups, postnatal survival Pup body weights decreased at all doses (females affected more than males) No effect on mating or fertility No effect on F2 litters Body weight was lower in females (5 and 15 mg/kg)

Lorcaserin Competition for [^{125}I]DOI Binding to Human 5-HT$_2$ Receptors



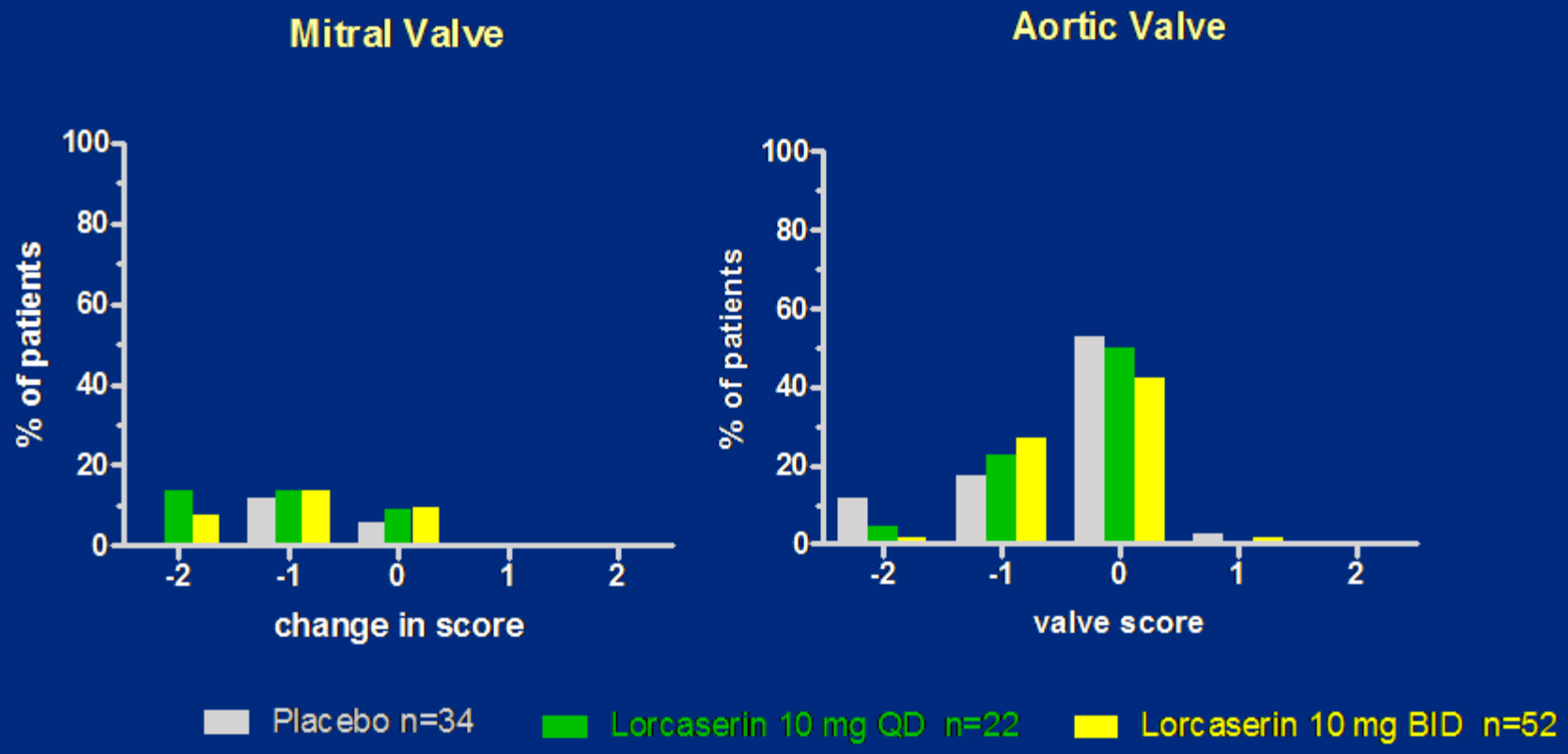
Serotonin Syndrome Patient Narrative (1 of 2)

- Patient 2109-S025 (APD356-011, lorcaserin 10 mg BID)
  - 29 y.o WF with h/o asthma and celiac sprue
  - Day 52: developed symptoms of URI and started a course of clarithromycin the next day (Day 53)
  - Day 57: took study drug and Mucinex DM (guaifenisen with dextromethorphan)
    - Approximately 30 min later developed vertigo, nausea, vomiting, diarrhea with some minor blood spots in stools, and BP increased to 135/105 (home reading); in clinic BP 100-122/75-80 on previous visits
    - Symptoms resolved after ~ 5 hrs but re-appeared with her evening dose of study drug and taking Mucinex DM again
    - Symptoms were resolved the next morning and she did not take study drug that morning

Serotonin Syndrome Patient Narrative (2 of 2)

- Week 8 clinic visit (Day 62): BP 110/80 and asymptomatic; Investigator diagnosed Serotonin Syndrome, moderate severity, probably related to study drug's interaction with dextromethorphan
  - Re-challenge with study drug was uneventful after holding study drug ~ 1 wk and discontinuing Mucinex DM
- Although the Investigator diagnosed serotonin syndrome, the event does not meet diagnostic criteria (only a single minor criterion, hypertension, was present)

Changes in Regurgitant Score at Index Valve in Patients with Baseline FDA-Defined Valvulopathy



Index valve refers to the valve that meets FDA-defined valvulopathy criteria

Co-Primary Endpoint #1
APD356-009 – MITT

	Placebo N=1499	Lorcaserin 10 mg BID N=1538
n (%) losing ≥5% weight	304 (20.3)	731 (47.5)
P-value		<0.0001

Change in Blood Pressure and Heart Rate from Baseline to Week 52: Responders vs. Non-Responders (MITT-LOCF)

	Responders		Non-Responders	
	Placebo N=682	10 mg BID N=1444	Placebo N=2098	10 mg BID N=1438
Mean (SD) Baseline SBP (mmHg)	123.2 (12.0)	122.0 (11.7)	121.0 (11.6)	120.9 (11.9)
Mean (SEM) Change	-3.8 (0.4)	-3.3 (0.3)	-0.2 (0.2)	-0.3 (0.3)
Mean (SD) Baseline DBP (mmHg)	78.1 (8.0)	77.7 (7.9)	77.6 (8.1)	77.2 (8.2)
Mean (SEM) Change	-2.9 (0.3)	-2.7 (0.2)	-0.5 (0.2)	-0.4 (0.2)
Mean (SD) Baseline Heart rate (bpm)	69.3 (8.6)	68.9 (8.9)	69.5 (9.0)	70.0 (8.6)
Mean (SEM) Change	-2.68 (0.36)	-2.25 (0.24)	0.23 (0.19)	-0.24 (0.22)

Ten Most Common AE Preferred Terms (%) by 5% Body Weight Responders (Yes, No), Pooled Phase 3

Preferred term	Placebo		Lorcaserin 10 mg QD		Lorcaserin 10 mg BID	
	No	Yes	No	Yes	No	Yes
Headache	10.0	10.5	17.1	13.3	16.3	17.4
Upper respiratory tract infection	10.9	17.3	13.4	16.5	11.9	15.9
Nasopharyngitis	11.0	15.3	9.8	15.2	10.2	16.2
Sinusitis	7.2	9.5	6.9	10.7	5.3	9.9
Nausea	5.6	4.4	8.5	6.1	7.7	8.9
Dizziness	3.4	5.4	6.1	6.5	6.9	10.3
Diarrhoea	5.0	8.0	7.5	5.2	4.7	8.6
Urinary tract infection	4.6	8.3	7.5	7.8	4.8	8.5
Back pain	5.2	7.0	5.9	8.4	4.3	8.6
Fatigue	3.6	3.5	7.3	5.5	6.1	8.5

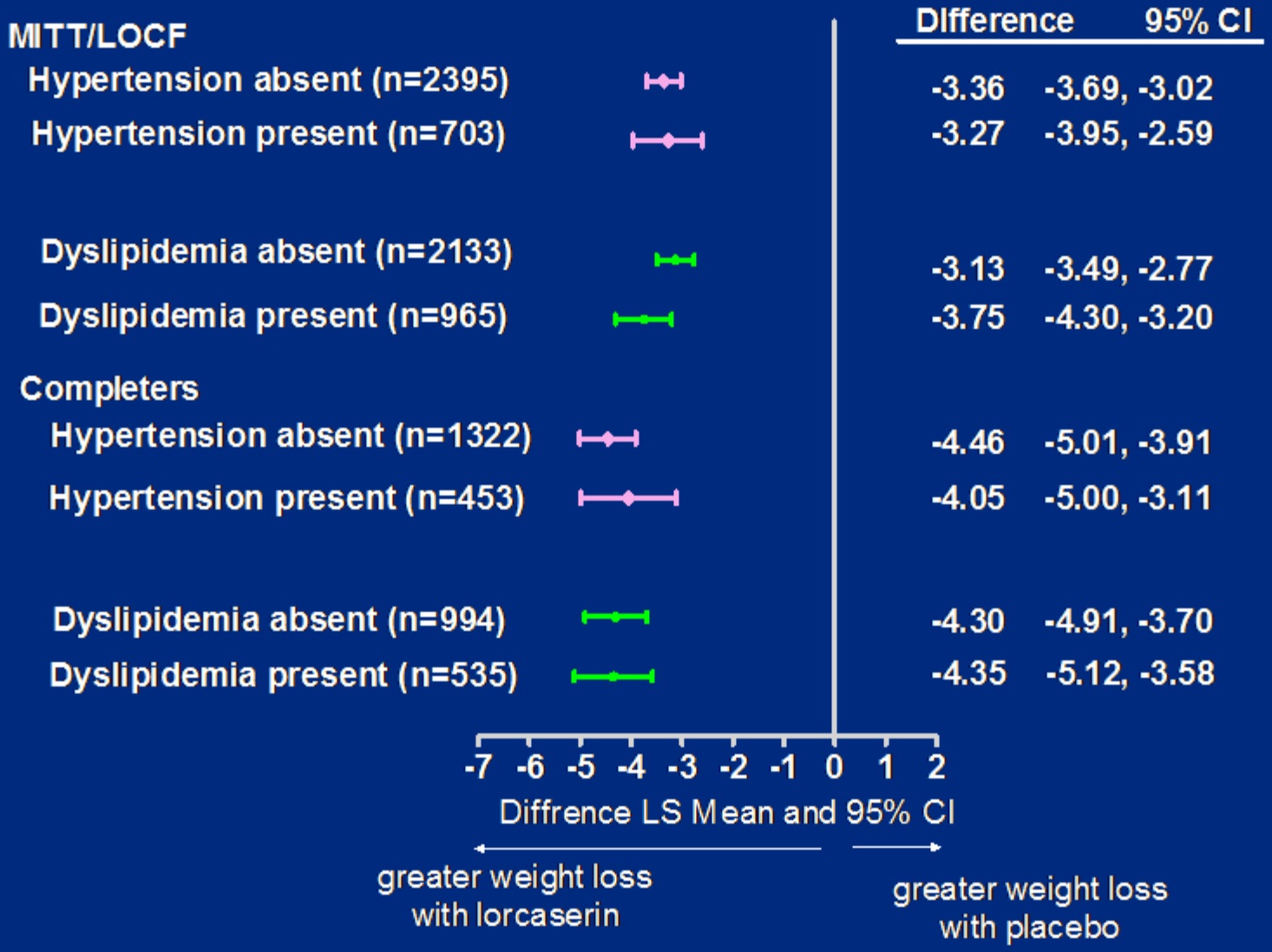
Note: 5% body weight responders were defined at Week 52 LOCF.

Patient Demographics Responders and Non-Responders

	Responders		Non Responders	
	Placebo (N=687)	10 mg BID (N=1460)	Placebo (N=2351)	10 mg BID (N=1638)
Mean (SD) Age, yrs	46.9 (11.5)	47.0 (10.6)	43.6 (11.3)	41.3 (11.6)
Mean BMI (SD), kg/m^2	35.8 (4.2)	35.8 (4.2)	36.1 (4.2)	36.4 (4.3)
Mean (SD) Weight, kg	99.4 (16.2)	99.0 (15.1)	100.5 (15.8)	101.6 (16.1)
Gender (%)				
Male	19.8	17.0	18.8	19.4
Female	80.2	83.0	81.2	80.6
Race (%)				
White	77.0	76.7	64.5	60.5
Black	12.1	13.7	20.6	23.0
Hispanic	9.5	7.3	12.8	14.2
Asian	0.6	0.8	0.6	0.7
Other	0.9	1.4	1.5	1.7

Note: Analysis was based on safety population.

Difference in Mean Change from Baseline in Body Weight (kg) at Week 52 by Baseline Co-morbidity: Pooled Phase 3 Studies



Results of Echo Variability Analysis using Screening Echocardiograms: Kappa Stats, APD356-009

Reader A versus Reader B, Difference between Reads

	N	Mean	SD	Minimum	Median	Maximum	Kappa (95% CI)
MR	3876	-0.11	0.65	-3.0	-	3.0	0.46 (0.44, 0.48)
AR	3858	-0.04	0.41	-3.0	-	2.0	0.43 (0.40, 0.47)

Change in Total Body Fat at Week 52: APD356-011

	Placebo	Lorcaserin 10 mg QD	Lorcaserin 10 mg BID
All Patients			
N	69	35	85
Mean (SD) Baseline, kg	45.0 (9.0)	45.7 (9.8)	44.5 (8.1)
Mean % (SEM) Change from Baseline	-4.6 (1.1)	-6.1 (2.0)	-9.9 (1.4)

Change in Lean Body Mass at Week 52: APD356-011

	Placebo	Lorcaserin 10 mg QD	Lorcaserin 10 mg BID
All Patients			
N	69	35	85
Mean (SD) Baseline, kg	51.0 (10.8)	48.2 (9.0)	48.0 (9.4)
Mean % (SEM) change from Baseline	-0.3 (0.4)	-2.0 (0.6)	-1.9 (0.5)